RESEARCH PROTECTIONS UPDATE

News and Comment on the Protection of Human Subjects in Navy and Marine Corps Research

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Commentary

Human Subject Research vs Quality Improvement

As often seen in healthcare settings today, clinicians assume several roles in their day to day responsibilities. They may be simultaneously functioning as healthcare providers, researchers and administrators. For those new to these roles (or even for those with many years of experience), the question may arise "is this project/activity I am about to embark upon, human subject research or QA/QI?" Quality Improvement (QI) and Quality Assurance (QA) are terms often used interchangeably (though incorrectly) to refer to the same concept. QI is more accurately a tool of QA, but for the purposes of this article the terms will be used synonymously as well. Differentiating between human subject research and QA/QI may be challenging. QA/QI is a critical part of hospital operation but methodologies associated with its implementation often intersect with research. Nonetheless, the goals of each endeavor are different and should not be confused. But why is this distinction necessary?

Although the methodologies may be similar; the purposes of human subject research and QA/QI differ and we are held to ethical and regulatory standards for human subject research, violations of which could lead to legal ramifications. Difficulty differentiating human subject research and QI is more prevalent when the project involves human participants and an intervention or interaction.

> *The traditional approach of distinguishing human subject research from QI using the Common Rule is a great and necessary starting point, however, the Common rule in itself is not robust enough to adequately describe the intricate differences between the two activities.*

The traditional approach of distinguishing human research from QI using the Common Rule is a great and necessary starting point; however, the Common rule in itself is not robust enough to adequately describe the intricate differences between the two activities. An in-depth look into regulations, pertinent instructions and guidance sets the foundation for a better understanding of each process and thus ultimately the differences between the two activities.

Spotlight

NMCP 4DX Project

By Kersten Wheeler

Naval Medical Center Portsmouth (NMCP) has built a culture of continuous process improvement using The 4 Disciplines of Execution (4DX) method based on the book (McChesney, Chris., Covey, Sean., Huling, Jim. The 4 Disciplines of Execution: Achieving Your Wildly Important Goals. New York: Free Press, 2012. Print.) NMCP holds training sessions and a 4DX summit twice a year to recognize the best projects from that cycle. In late 2015, the Research Subjects Protection Division (RSPD) within the Clinical Investigation Department (CID) was asked to participate in the program.

Our project was called "Clearing hurdles to approval." Before new IRB protocols can be initiated at NMCP, they are individually

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Also in this Issue:

Flashback

Henry K. Beecher: Over 50 years since his influential paper "Ethics and Clinical Research"

Henry K. Beecher was a highly respected anesthesiologist and medical ethicist born in Peck, Kansas 1904. He obtained a BA degree and MA degree in chemistry prior to enrolling in Harvard Medical School. He obtained his medical degree from Harvard, graduating cum laude in 1932 and served in the U.S Army during World War II. Henry Beecher returned to Harvard after WWII and closely followed the Nuremberg Trials, developing and refining his beliefs on the ethical conduct of human subject research. Preceding his seminal publication in 1966, Henry Beecher wrote and published several other articles regarding ethical issues in human subject clinical research.

"Ethics and Clinical Research" was published on June 16, 1966 in the New England Journal of Medicine. In this landmark publication, Henry Beecher cited 22 examples of human subject research misconduct. This paper has been lauded as "...the most influential single paper ever written about experimentation involving human subjects." [1] Included in the 22 examples cited are the now infamous Tuskegee syphilis, Willowbrook and Jewish Chronic Disease Hospital studies. Public reaction to this paper was significant with stories in the Boston Globe, Wall Street Journal and others. Beecher's groundbreaking paper influenced the implementation of Federal rules governing human subject research. Following its publication, the Federal Protections for Human Subjects was established in 1974 and the Belmont Report followed in 1979. The lasting legacy of this paper is summarized by DJ Rothman : "At least, researchers today would not consider submitting protocols like those in Beecher's list of 22. At most, more subjects are giving truly informed consent."[2]

References:

1. Harkness J, Lederer S, Wikler D. Laying ethical foundation for clinical research." Bulletin of the World Health Organization 2001; 79(4): 365-366
2. Rothman DJ. Ethics and human experimentation: Henry Beecher revisited. NEJM 1987; 317: 1195-1199

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What do the regulations, guidance and instructions say about human subject research and QA/QI ?

The Common Rule, codified in title 32 CFR 219 for the Department of Defense (DoD), defines research as a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. It describes human subject as "a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or identifiable private information." [1] Research regulation does not include QA/QI in its scope of definitions, so we must look to other sources for descriptions of this activity. The Department of the Navy (DON) provides instruction on QA/QI in medical treatment facilities. BUMED Instruction 6010.13 defines QA/QI "as the formal and systematic exercise of monitoring and reviewing medical care delivery and outcome; designing activities to improve health care and overcome identified deficiencies in providers, facilities, or support systems; and carrying out follow-up steps or procedures to ensure the actions have been effective, that no new problems have been introduced, and that individual improvements in quality as a result of process improvement is maintained."[2] The U.S Department of Health and Human Services Health Resources and Services Administration established guidance on QA/QI published April, 2011. In this guidance it states, "QI consists of systematic and continuous actions that leads to measurable improvement in health care services and health status of targeted patient groups." [3] QI projects or activities are generally part of an institution's quality management/quality assurance (QA) program effort to

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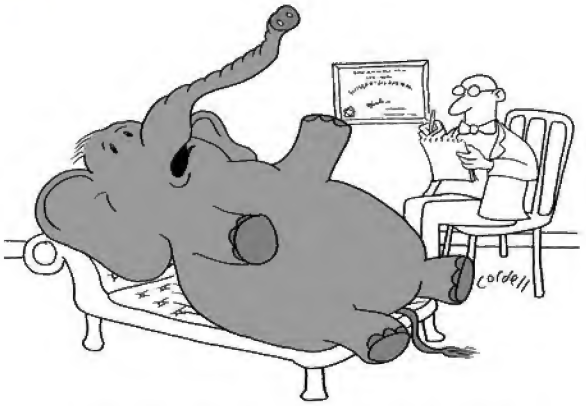
identify and make improvements in patient healthcare based on data collection, analysis and intervention. Thus QA/QI is driven by the need to improve process and performance within an institution while research is motivated by the need to test a hypothesis or answer a research question with the intent to contribute to generalizable knowledge. QI projects in healthcare are varied covering administrative, clinical and a spectrum of directives that falls in between. Similar to human subject research, QI projects also employ a variety of methodologies and data collection may be prospective or retrospective to include data on processes or outcomes. [4]

Starting with the regulatory definition of research, the following questions should be asked to begin in making a distinction between human subject research and QI:

1. Does the activity involve research per 32 CFR 219.102(d)? Is this activity a systematic investigation (testing or evaluation) designed to contribute to generalizable knowledge? (continued on page 6)

Common Rule Buzz

The Elephant in the Room



So we can't ignore the proverbial "elephant in the room." The revised Common Rule was initially set with a compliance date of January 19, 2018. As you may or may not have heard, the Association of American Medical Colleges (AAMC), Association of American Universities (AAU), Association of Public & Land-grant Universities (APLU) and Council on Governmental Relations (COGR) wrote a letter[1] to HHS in June, 2017, requesting a one year delay in the compliance date of the revised Common Rule. On 17 January 2018, the Department of Health and Human Services announced an Interim Final Rule that delays by six months (19 July 2018) the effective date and general compliance date of the revisions to the Common Rule.[2] This delay has significant implications for DON research. While we continue to comply with the existing Common Rule, we now have more time to prepare for the impact the revisions will have on our HRPPs. This means more time to think about the changes and how it affects our processes. We also would have more time for education and establishment of policies and procedures to ensure compliance with the revisions.

We understand there has been some hesitation in proceeding with preparations due to uncertainty regarding the status of the revised Common Rule. Also, we have all been expecting further guidance from higher authorities to help better understand how the revisions are to be implemented. This delay is a welcome relief as it allows more time for guidance to be provided. Stay tuned!

Resources:

1. http://www.cogr.edu/sites/default/files/AAMC_AAU_APLU_COGR%20Common%20Rule%20Delay%20Letter%206-21-2017.pdf
2. https://www.federalregister.gov/documents/2018/01/22/2018-00997/federal-policy-for-the-protection-of-human-subjects-delay-of-the-revisions-to-the-federal-policy-for

NMCP4DX Project

By Kersten Wheeler *(continued from page 1)*

sent to the commanding officer for his review and approval.

In addition, the NMCP IRB processes more than 100 post-approval actions (amendments, continuing reviews, etc.) each month that also require commanding officer review and approval. Instead of sending these items individually to the commanding officer, they are packaged in the reporting section of the meeting minutes, which are then sent for leadership approval.

A "Wildly Important Goal," or WIG for short, is a tactical goal with a limited time frame. Our WIG was to decrease the time from IRB meetings to the release of approved items to investigators by 20 percent within six months. Tracking of the IRB minutes was used to measure the approval process and facilitate this goal. Prior to starting the project, the average approval time was 28 days. We wanted to streamline the approval process to improve researcher satisfaction and meet or exceed industry standards. Furthermore, by decreasing the approval time of the minutes, we wanted to increase the number of research activities within Navy Medicine East by providing faster turnaround times between project conception to protocol implementation. To attain the WIG and win the "war," we broke the project up into three lead measures or "battles" with their own optimized timeframes. Our first battle was to draft the minutes within three business days of a convened IRB meeting. Secondly, within three more days the meeting minutes were to be electronically reviewed by the IRB Chair, the Head of CID, and the Head of RSPD. Lastly, within one day, RSPD would then hand-deliver a hard copy of the meeting minutes to the Command Suite for review and approval. We developed a scoreboard poster to represent our project and used hurdles to represent our progress (see picture). If we won our individual battles each month, the hurdles remained standing. If we were unsuccessful, the hurdles were knocked down. The poster provided a real-time visual of how our project was proceeding each month. We displayed in it our department lobby so that we could share our progress with our colleagues and to keep us motivated to conquer all of our battles. There were times we struggled to hit all of our targets, which required us to adjust our internal processes to reach our end goals. We were able to defeat all of our battles to win the war! We exceeded each of three smaller goals along with exceeding our overall WIG.

At the end of the project, our minutes were drafted (on average) in 1.2 days. Our minutes review was completed within 2.92 days, and our minutes were typically delivered to the commanding officer within a matter of hours. Before this project our time to Principal Investigator (PI) notification was 27.9 days. Now time to PI notification is 10.7 days. This is a difference of 17.2 days, which equals a 61.6 percent decrease in approval time! We significantly surpassed our original goal of reducing the overall time by 20 percent. We were invited to share our results with command leadership at the April 2016 4DX Summit where we received an overwhelming amount of positive feedback on our project.

We certainly exceeded our original goals and have greatly streamlined our approval process. All of our RSPD staff were integral to the triumph of the project. The team was dedicated to every phase of the project including designing the project goals, attending 4DX training, creating the scoreboard and, most importantly, implementing methods to improve every step of the approval process. We have created an efficient process that we continue to maintain.

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NMCP 4DX Project *(continued)*

From left to right; Kersten Wheeler, Paulette Mitchell, Dr. Thomas Rieg, Elizabeth Dayag and Melvina Queen of NMCP Research Subject Protections Division receiving Letters of Commendation from CO CAPT Christopher M. Culp for the 4DX project.

DON HRPP News

Please help us welcome the following new members to the DON HRPP team!

Amber Gunn Westland: Human Research Protection Specialist
Bridget Newell: Human Research Protection Specialist
Chidima Ioanou: Human Research Protection Specialist (Training and Education)
John Morais: Human Research Protection Specialist
Paige Lispcome: Human Research Protection Specialist

We Need Your Help!

Get a BZ from RPU

Have a "Good News" story or picture from your Research Protection Program? Don't keep it to yourself! Why not share it with the DON Research Protection community? We're looking for material to publish in the *Research Protections Update* newsletter. Send your research news, success stories, tips, pictures, lessons learned, or other material related to the ethical conduct of human research to usn.ncr.bumedfchva.mbx.don-hrpp@mail.mil

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2. Does this activity involve human subjects per 32 CFR 219.102(f)? Is the investigator conducting research gathering data about living individuals? Will the investigator gather data through either of the following mechanisms: physical procedures or manipulation of those individuals or their environment (intervention) or communication or interpersonal contact with the individuals (interaction)? Or will the investigator gather identifiable data?

If the answers to both questions are "yes," IRB review or making exempt determination is required and the activity may be determined exempt, expedited or needing a convened full board review. If the answer to question 1 is a "yes," but the answer to question 2 is "no," IRB review is not required and the activity is considered to be not human subject research. If you are considering a QA/QI activity and the answers to both questions are definitively "no," then it is not human subject research and the activity may be a QA/QI project purposed to evaluate a system or process for application at a local level.

What is OHRP's stance on human subject research vs QA/QI?

OHRP does not have an official guidance document differentiating quality improvement versus human subject research. However, there are a few published statements on the matter from which their stance can be surmised. OHRPs webpage "Quality Improvement FAQs" [5] and correspondence titled "Indwelling Catheter QI procedures: Letter, July 30, 2008" [6] sheds some light on differentiating human subject research from QI. Differences highlighted include the purpose, design, publication of findings and applicability of IRB review and determinations. OHRP's stance on QA/QI is that it should be limited to implementing a practice or data collection (on patient or provider) to improve quality of patient care for clinical, practical and administrative purposes. OHRP also provides guidance on publication of findings, stating intent to publish is not a determining factor in distinguishing QI from research. OHRPs "Quality Improvement FAQs" answers questions and provides examples to help understand the difference between human subject research and QA/QI. An example provided posits a QI project designed to improve patient outcome as well as answer a research question. The exemplified project involves an untested clinical intervention purposed to improve quality of care but also collects information about patient outcomes for the purposes of establishing scientific evidence to determine how well the intervention achieves its intended results. Hence, to clarify, some QI projects may indeed also be non-exempt human subject research requiring IRB review. Notably in the OHRP's correspondence titled "Indwelling Catheter QI procedures: Letter, July 30, 2008", a more detailed example of a QI project designed to also include human subject research is provided. This project was a five part program implemented in various hospitals to reduce catheter-related blood stream infections. Data to be collected included; 1) number of infections, 2) number of catheter days, 3) data gathered through surveys of staff (not identified by individual respondent) regarding perceptions of culture safety in the ICU and 4) data gathered through survey of staff on perceptions on the process of implementing the program (also not identified by individual respondent). OHRP made the following analysis of how the regulations for human subject protections applied to this project:

OHRP's stance on QA/QI is that it should be limited to implementing a practice or data collection (on patient or provider) to improve quality of patient care for clinical, practical and administrative purposes.

1. Across all participating institutions, the implementation of the five part catheter-related bloodstream infection reduction program is a QA/QI activity. This is because the program is being implemented to improve quality of healthcare and not to evaluate effectiveness. Thus this activity does not meet the

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regulatory definition of human subject research.

2. The collection and analysis of aggregate data on number of infections and number of catheter days does not fall under the regulation definition of human subject research under 45 CFR 43.102(f). This is because identifiable private information about living individuals is not being obtained nor is there an intervention or interaction with living individuals for research purposes.

3. The collection of data through the two surveys does fall under human subject research per regulatory definition. However, since the surveys are not identified by individual respondent and is being collected anonymously this research activity is exempt from the regulatory requirements under 45 CFR 46.101(b)(2).

So, how do we make sense of this information and what should we do?

Taking applicable regulation, instruction and guidance into consideration, we should also carefully consider intent, design, effect on program or practice and planned dissemination of results of the project during it's conception to help in differentiating human subject research from QA/QI. [7] Human subject research and QA/QI are both vital parts of healthcare. It is essential that human subject research and QA/QI be distinguished so that IRB review of research can be implemented to conduct risk level determination and review all other research related documents and processes to ensure subject safety. It is also important that areas for QI be identified, data collected, intervention evaluated and improvements implemented in a timely manner for healthcare improvements. [8] Both activities are mandatory elements integrated into clinical operations in order to facilitate excellence in the delivery of patient care and improved health outcomes. We are held to ethical and regulatory standards during implementation of these activities. Thus, the need for regular discussion and education of this topic is very much warranted.

The difference between QI and research is not always straightforward…when in doubt some investigators may be tempted to pursue the route of quality improvement because institutional approval may be easier and quicker. This is not an appropriate response to the dilemma. Follow your institution guidelines and consult with your Institution's IRB, local Human Research Protection Program or DON HRPP to ensure compliance with human research protections.

References

1. 32 CFR 219: https://www.ecfr.gov/cgi-bin/text-idx?SID=93870c200ce2cdbd5c53d2da1fa01e12&mc=true&node=pt32.2.219&rgn=div5#se32.2.219_1101
2. HHS HRSA Quality Improvement: https://www.hrsa.gov/sites/default/files/quality/toolbox/508pdfs/qualityimprovement.pdf
3. The Hastings Center, Health Care Quality Improvement: Ethical and Regulatory Issues: http://www.thehastingscenter.org/wp-content/uploads/Health-Care-Quality-Improvement.pdf
4. BUMED Instruction 6010.13 Quality Assurance: http://www.med.navy.mil/directives/ExternalDirectives/6010.13.pdf
5. OHRP Quality Improvement FAQs: https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/quality-improvement-activities/index.html
6. OHRP Correspondence; Indwelling Catheter QI Procedures: Letter, July 30, 2008: https://www.hhs.gov/ohrp/regulations-and-policy/guidance/july-30-2008-letter-to-dr-peter-provonost/index.html
7. DHA Humans Subject Research versus QI Activity: https://www.health.mil/Reference-Center/Fact-Sheets/2015/10/13/Human-Subjects-Research-versus-Quality-Improvement-Activities
8. https://www.ncbi.nlm.nih.gov/pubmed/12400106

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